paragraph, because the specification is deemed to be enabling for a polypeptide comprising the amino acid sequence of SEQ ID NO: 5 but not for variants or fragments of the polypeptide of SEQ ID NO: 5. The Action states that in the absence of explicit disclosure regarding the biological activity or essential characteristics of IFN-L polypeptide, it is unpredictable as to which variants and fragments would have the properties of IFN-L polypeptide, and that it would, therefore, require undue experimentation to make and use the invention.

Applicants contend that the specification does indeed set forth a particular biological activity for IFN-L polypeptides at page 103, lines 19-27, in an Example entitled "Biological Activity of IFN-L Polypeptides." Specifically, the specification discloses that when several cell lines were exposed to a rat IFN-L-Fc fusion polypeptide, an increase in cellular protein tyrosine phosphorylation was detected. Applicants also note that interferons are known to activate gene transcription by acting through a signaling pathway involving cell-surface receptors, tyrosine kinases, and cytoplasmic transcription factors (Shuai, 1994, *Curr. Opin. Cell Biol.* 6:253-59; Gilmour *et al.*, 1995, *Gene Expr.* 5:1-18; Larner *et al.*, 1996, *Biotherapy* 8:175-81). For example, in the IFN-γ signaling pathway, IFN-γ first binds the IFN-γ receptor, resulting in the phosphorylation of two members of the Janus tyrosine kinase (JAK) family, Jak1 and Jak2 (Pestka, 1997, *Semin. Oncol.* 24(3 Suppl. 9):S9-18-S9-40). The JAK kinases, in turn, phosphorylate the IFN-γ receptor, which then serves as a recruitment site for a member of the signal transducers and activators of transcription (STAT) family, Stat1α (Pestka, 1997). Following recruitment, Stat1α is phosphorylated and then released as an active transcription factor for IFN-γ-induced genes (Pestka, 1997). Analogous signaling pathways have been delineated for IFN-α, IFN-β, and IFN-ω, wherein the binding of interferon to a cell-surface receptor leads to the activation of JAK tyrosine kinases and the subsequent phosphorylation of STAT cytoplasmic transcription factors (Gilmour *et al.*, 1995; Larner *et al.*, 1996; Pestka, 1997; Heim, 1999, *J. Recept. Signal Transduct. Res.* 19:75-120).

The specification provides teachings regarding the mature form of human IFN-L polypeptide (Figures 2A-2B), the preparation of IFN-L polypeptide variants having conservative amino acid substitutions (page 23, lines 2-12), and examples of appropriate hybridization conditions for identifying IFN-L polypeptide variants (*e.g.*, page 17, lines 7-10; page 18, lines 11-13). Applicants contend that based on the specification's teaching, one of ordinary skill in the art would readily be able to determine which IFN-L polypeptide variants and fragments cause an increase in cellular

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protein tyrosine phosphorylation, and therefore, that it would not require undue experimentation for one of ordinary skill in the art to determine which IFN-L polypeptide variants and fragments have the properties of IFN-L polypeptide. Applicants, therefore, respectfully request that this rejection be withdrawn.

The Office Action also asserts a rejection of claims 1, 2, 4, 7-9, 11-17, 19, and 20 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Action states that Applicants' referral to the deposit of PTA-976 in the specification is an insufficient assurance that all of the conditions of 37 C.F.R. §§ 1.801-1.809 have been met, and that an affidavit or declaration by Applicants, their assignee, or an attorney of record over his or her signature and registration number, stating that a deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposited material will be irrevocably removed upon the granting of a patent on this application, and that the deposited material will be replaced if viable samples cannot be dispensed by the depository, is required. The Action also states that the specification must be amended to recite the date of deposit, the complete name and address of the depository, and the accession number of the deposited biological material.

Applicants respectfully direct the Examiner's attention to page 92, lines 25-28 of the specification where Applicants disclose that a deposit of cDNA encoding human IFN-L polypeptide, subcloned into pSPORT1 (Gibco BRL) and transformed into *E. coli* strain DH10B, was made with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, before the filing date of the instant application. Pursuant to the Examiner's request, Applicants also submit herewith a Declaration stating that deposits complying with 37 C.F.R. §§ 1.801-1.809 were made under the provisions of the Budapest Treaty. Applicants contend that all the requirements of 37 C.F.R. §§ 1.801-1.809 have been met. *In re Lundak,* 225 U.S.P.Q. 90 (Fed. Cir. 1985). Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 2-9 and 11-20 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that while the specification discloses

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two polynucleotides encoding two polypeptides, the claims encompass a broad genus of polypeptides that vary substantially in length and composition, including fragments, molecules with limited homology, and molecules having an unlimited number of truncations, deletions, and insertions. The Action also states that the specification fails to provide sufficient guidance regarding the common attributes or characteristics that identify members of the claimed genus – such as conserved regions that are critical to IFN-L polypeptide function or residues where variability would be tolerated. The Action further states that in the absence of a description of the definitive structural or functional features of the claimed genus, one of ordinary skill in the art would not be able to determine which molecules fall within the scope of the claims. In particular, the Action states that the specification fails to sufficiently describe a genus that encompasses allelic variants and splice variants.

Applicants have amended claim 2 to recite an isolated polypeptide comprising an amino acid sequence as set forth in SEQ ID NO: 6, optionally further comprising an amino-terminal methionine; an amino acid sequence that is at least about 70 percent identical to the amino acid sequence set forth in SEQ ID NO: 5, wherein the polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation; or a fragment of the amino acid sequence set forth in SEQ ID NO: 5 comprising at least about 25 amino acid residues, wherein the polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation. Applicants note that amended claim 2 no longer recites an amino acid sequence for an ortholog of SEQ ID NO: 5 or an amino acid sequence for an allelic variant or splice variant of the amino acid sequence as set forth in SEQ ID NO: 5 or the amino acid sequence encoded by the DNA insert in ATCC Deposit No. PTA-976. Applicants thus contend that amended claim 2 does not encompass a broad genus of polypeptides that vary substantially in length and composition. Further, in view of the teachings in their specification of the amino acid sequence for human IFN-L polypeptide (Figures 2A-2B), the mature form of human IFN-L polypeptide (Figures 2A-2B), and the biological activity of IFN-L polypeptide (page 103, lines 19-27), one of ordinary skill in the art would understand the scope of species comprising the disclosed genus, and that the inventors were in possession of the invention having said scope at the time the application was filed. Applicants respectfully request that this ground of rejection, as it applies to claim 2, be withdrawn.

Applicants have amended claim 3 to recite an isolated polypeptide comprising an amino acid sequence as set forth in SEQ ID NO: 5 with at least one conservative amino acid substitution or

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having a C- and/or N- terminal truncation, wherein the polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation. Applicants note that amended claim 3 no longer recites an amino acid sequence as set forth in SEQ ID NO: 5 with at least one insertion or one deletion. Applicants also note that the specification teaches the amino acid sequences for rat and human IFN-L polypeptide (Figures 1A-1B and 2A-2B), an amino acid sequence alignment demonstrating that rat and human IFN-L polypeptide share amino acid sequence identity with human IFN-β (Figure 3), that regions in IFN-L polypeptide that are tolerable to conservative amino acid substitution can be identified by performing sequence comparisons between IFN-L polypeptide and other related polypeptides (page 23, lines 2-12), rubrics recognized in the art for making conservative amino acid substitutions (Table 1, pages 21-22), and the biological activity of IFN-L polypeptide (page 103, lines 19-27). Applicants, therefore, contend that amended claim 3 does not encompass a broad genus of polypeptides that vary substantially in length and composition, and that in view of the specification's teachings, one of ordinary skill in the art would understand the scope of species comprising the disclosed genus, and that the inventors were in possession of the invention having said scope at the time the application was filed. Applicants respectfully request that this ground of rejection, as it applies to claim 3, be withdrawn.

Applicants have amended claim 4 to recite an isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence as set forth in SEQ ID NO: 4; of the DNA insert in ATCC Deposit No. PTA-976; encoding a polypeptide as set forth in SEQ ID NO: 5; or that hybridizes to the complement of either of these nucleotide sequences under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences, wherein the encoded polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation. Applicants note that claim 16 has been similarly amended. Applicants also note that the specification teaches the nucleotide sequence for human IFN-L polypeptide (Figures 2A-2B), examples of appropriate hybridization conditions for identifying IFN-L polypeptide variants (page 18, lines 11-13), and the biological activity of IFN-L polypeptide (page 103, lines 19-27). Applicants, therefore, contend that neither claim 4 nor claim 16, as amended, encompass a broad genus of polypeptides that vary substantially in length and composition, and that in view of the specification's teachings, one of ordinary skill in the art would understand the scope of species comprising the disclosed genus, and that the inventors were in possession of the invention having said scope at the

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time the application was filed. Applicants respectfully request that this ground of rejection, as it applies to claims 4 and 16, be withdrawn.

Applicants have amended claim 5 to recite an isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide that is at least about 70 percent identical to the polypeptide set forth in SEQ ID NO: 5, wherein the encoded polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation; a region of the nucleotide sequence of SEQ ID NO: 4, the DNA insert in ATCC Deposit No. PTA-976, or the nucleotide sequence of (a), wherein the encoded polypeptide comprises at least about 25 amino acid residues, and wherein the encoded polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation, or is antigenic; or a nucleotide sequence that hybridizes to the complement of the preceding nucleotide sequence under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences, wherein the encoded polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation. Applicants note that amended claim 5 no longer recites an isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in SEQ ID NO: 4 or the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-976; or a region of the nucleotide sequence of SEQ ID NO: 4 or the DNA insert in ATCC Deposit No. PTA-976, comprising a fragment of at least about 16 nucleotides. Applicants also note that claim 17 has been similarly amended. Applicants further note that the specification teaches the nucleic sequence for human IFN-L polypeptide (Figures 2A-2B), examples of appropriate hybridization conditions for identifying IFN-L polypeptide variants (page 18, lines 11-13), and the biological activity of IFN-L polypeptide (page 103, lines 19-27). Applicants, therefore, contend that neither claim 5 nor claim 17, as amended, encompass a broad genus of polypeptides that vary substantially in length and composition, and that in view of the specification's teachings, one of ordinary skill in the art would understand the scope of species comprising the disclosed genus, and that the inventors were in possession of the invention having said scope at the time the application was filed. Applicants respectfully request that this ground of rejection, as it applies to claims 5 and 17, be withdrawn.

Applicants have amended claim 6 to recite an isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 5 with

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at least one conservative amino acid substitution; having a C- and/or N- terminal truncation; or that hybridizes to the complement of either of these nucleotide sequences under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences; wherein the polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation. Applicants note that amended claim 6 no longer recites an isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 5 with at least one insertion or one deletion. Applicants also note that claim 18 has been similarly amended. Applicants further note that the specification teaches the amino acid sequences for rat and human IFN-L polypeptide (Figures 1A-1B and 2A-2B), an amino acid sequence alignment demonstrating that rat and human IFN-L polypeptide share amino acid sequence identity with human IFN-β (Figure 3), that regions in IFN-L polypeptide that are tolerable to conservative amino acid substitution can be identified by performing sequence comparisons between IFN-L polypeptide and other related polypeptides (page 23, lines 2-12), rubrics recognized in the art for making conservative amino acid substitutions (Table 1, pages 21-22), examples of appropriate hybridization conditions for identifying IFN-L polypeptide variants (page 18, lines 11-13), and the biological activity of IFN-L polypeptide (page 103, lines 19-27). Applicants, therefore, contend that neither claim 6 nor claim 18 encompass a broad genus of polypeptides that vary substantially in length and composition, and that in view of the specification's teachings, one of ordinary skill in the art would understand the scope of species comprising the disclosed genus, and that the inventors were in possession of the invention having said scope at the time the application was filed. Applicants respectfully request that this ground of rejection, as it applies to claims 6 and 18, be withdrawn.

With regard to the Action's rejection of claims 2-9 and 11-20 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, Applicants contend that claims 2-9 and 11-20, as amended, do not encompass a broad genus of polypeptides that vary substantially in length and composition, and that in view of the specification's teachings, one of ordinary skill in the art would understand the scope of species comprising the disclosed genus, and that the inventors were in possession of the invention having said scope at the time the application was filed. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

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Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

2. Rejections of claims 2-9 and 11-20 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 2-9 and 11-20 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

The Action first asserts that claim 2 is indefinite for reciting the term "ortholog" because the term is not defined in the specification, and in the absence of such a definition, one of ordinary skill in the art would not be able to determine which molecules fall with the scope of the claims. While Applicants note that the specification defines the meaning of the term "IFN-L polypeptide ortholog" (page 12, lines 1-4), Applicants have amended the pending claims without prejudice or disclaimer in an effort to expedite the present application to allowance. Applicants respectfully contend that because the amended claims no longer recite IFN-L polypeptide orthologs, this ground of rejection should be withdrawn.

The Action next asserts that claims 4-6 and 16-18 are indefinite for reciting molecules identified by hybridization because hybridization conditions are not defined in the specification, and in the absence of such a definition, one of ordinary skill in the art would not be able to determine which molecules fall with the scope of the claims. Applicants have amended claims 4-6 and 16-18 to encompass molecules identified by hybridization "under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences." Applicants contend that the skilled artisan could use the teachings of the specification and knowledge in the art to determine hybridization conditions in which "no more than a 21% mismatch between the nucleotide sequences" was obtained. For example, the specification discloses that when hybridization is performed at 50°C in a buffer containing 0.015 M Na^+, such results can be obtained (page 18, lines 13-14). Applicants also contend that one of ordinary skill in the art would appreciate that such results can be obtained using the same Na^+ concentration and lower temperatures, provided that a denaturing agent (such as formamide) is added to the hybridization buffer. *See, e.g.*, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual* 6.59-6.60 (3rd ed. 2001) (describing an equation for determining the melting temperature of

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duplex DNA in a hybridization buffer containing formamide), a copy of which is enclosed. Applicants contend that the amended claims satisfy the requirements of 35 U.S.C. § 112, second paragraph, and therefore, respectfully request withdrawal of this rejection.

The Action next asserts that claims 2-6, 17, and 18 are indefinite for reciting the phrase "has an activity of the polypeptide set forth in...SEQ ID NO: 5" because such activities are not set forth in the specification. As discussed in section 1, stimulation of protein tyrosine phosphorylation is a characteristic functional property of interferons. Applicants contend that the specification clearly discloses that the IFN-L polypeptides of the invention possess this characteristic functional property. Applicants have amended claims 2-6, 17, and 18 to replace the limitation "has an activity of the polypeptide set forth in...SEQ ID NO: 5," with the requirement that the claimed IFN-L polypeptides exhibit the characteristic interferon activity of increasing cellular protein tyrosine phosphorylation. Applicants contend that the amended claims satisfy the requirements of 35 U.S.C. § 112, second paragraph, and therefore, respectfully request withdrawal of this rejection.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

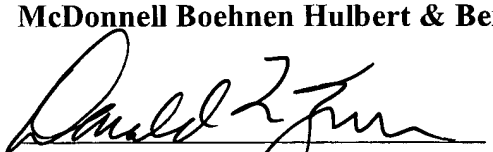
CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Andres believes it to be helpful, she is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: February 19, 2003

By: 
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AMENDMENTS TO THE CLAIMS

Marked Up Versions of Amended Claims under 37 C.F.R. 1.121(c)(1)(ii)

1. (Amended) An isolated polypeptide comprising an amino acid sequence ~~selected from the group consisting of~~:

(a) ~~the amino acid sequence~~ as set forth in ~~either SEQ ID NO: 2 or~~ SEQ ID NO: 5; ~~and~~ or

(b) ~~the amino acid sequence~~ encoded by the DNA insert in ATCC Deposit No. PTA-976.

2. (Amended) An isolated polypeptide comprising ~~an amino acid sequence selected from the group consisting of~~:

(a) ~~the~~ an amino acid sequence as set forth in ~~either SEQ ID NO: 3 or~~ SEQ ID NO: 6, optionally further comprising an amino-terminal methionine;

~~(b) an amino acid sequence for an ortholog of either SEQ ID NO: 2 or SEQ ID NO: 5;~~

~~(c)~~(b) an amino acid sequence that is at least about 70 percent identical to the amino acid sequence ~~of either SEQ ID NO: 2 or~~ set forth in SEQ ID NO: 5, wherein the polypeptide ~~has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~ upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation; or

~~(d)~~(c) a fragment of the amino acid sequence set forth in ~~either SEQ ID NO: 2 or~~ SEQ ID NO: 5 comprising at least about 25 amino acid residues, wherein the polypeptide ~~fragment has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~ upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation, or is antigenic; ~~and~~

~~(e) an amino acid sequence for an allelic variant or splice variant of the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 5, the amino acid sequence encoded by the DNA insert in ATCC Deposit No. PTA-976, or the amino acid sequence of any of (a) - (c)~~.

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3. (Amended) An isolated polypeptide comprising an amino acid sequence ~~selected from the group consisting of~~ as set forth in SEQ ID NO: 5:

(a) ~~the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~ with at least one conservative amino acid substitution~~, wherein the polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~;

~~(b) the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 5 with at least one amino acid insertion, wherein the polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5;~~

~~(c) the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 5 with at least one amino acid deletion, wherein the polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5;~~

~~(d)~~(b) ~~the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 5 that has~~ving a C- and/or N- terminal truncation~~, wherein the polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5; and~~ or

~~(e)~~(c) ~~the amino acid sequence as set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~ with at least one modification ~~selected from the group consisting of~~ that is a conservative amino acid substitution~~s, amino acid insertions, amino acid deletions~~, C-terminal truncation, ~~and~~ or N-terminal truncation~~;~~;

wherein the polypeptide ~~has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~ upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation.

4. (Amended) An isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence ~~selected from the group consisting of~~:

(a) ~~the nucleotide sequence~~ as set forth in ~~either SEQ ID NO: 1 or~~ SEQ ID NO: 4;

(b) ~~the nucleotide sequence~~ of the DNA insert in ATCC Deposit No. PTA-976;

(c) ~~a nucleotide sequence~~ encoding ~~the~~ a polypeptide as set forth in ~~either SEQ ID NO: 2 or~~ SEQ ID NO: 5; ~~and~~ or

(d) ~~a nucleotide sequence~~ that hybridizes ~~under at least moderately stringent conditions~~ to the complement of the nucleotide sequence of any of (a) - (c) under hybridization

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conditions allowing no more than a 21% mismatch between the nucleotide sequences;,

wherein the encoded polypeptide ~~has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~ upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation.

5. (Amended) An isolated polypeptide encoded by a nucleic acid molecule comprising ~~a nucleotide sequence selected from the group consisting of~~:

(a) a nucleotide sequence encoding a polypeptide that is at least about 70 percent identical to the polypeptide ~~as~~ set forth in ~~either SEQ ID NO: 2 or~~ SEQ ID NO: 5, wherein the encoded polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation;

~~(b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in either SEQ ID NO: 1 or SEQ ID NO: 4, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-976, or the nucleotide sequence of (a);~~

~~(c)~~(b) a region of the nucleotide sequence of ~~either SEQ ID NO: 1 or~~ SEQ ID NO: 4, the DNA insert in ATCC Deposit No. PTA-976, or the nucleotide sequence of (a) ~~or (b)~~, wherein the encod~~inged a~~ polypeptide ~~is a fragment of~~ comprises at least about 25 amino acid residues, and wherein the encoded polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation, or is antigenic; or

~~(d) a region of the nucleotide sequence of either SEQ ID NO: 1 or SEQ ID NO: 4, the DNA insert in ATCC Deposit No. PTA-976, or the nucleotide sequence of any of (a) - (c), comprising a fragment of at least about 16 nucleotides; and~~

~~(e)~~(c) a nucleotide sequence that hybridizes ~~under at least moderately stringent conditions~~ to the complement of the nucleotide sequence of ~~any of (a) - (d)~~ (b) under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences;,

wherein the encoded polypeptide ~~has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~ upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation.

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6. (Amended) An isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence ~~selected from the group consisting of~~:

(a) ~~a nucleotide sequence~~ encoding a polypeptide as set forth in ~~either SEQ ID NO: 2 or~~ SEQ ID NO: 5 with at least one conservative amino acid substitution;

~~(b) a nucleotide sequence encoding a polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 5 with at least one amino acid insertion;~~

~~(c) a nucleotide sequence encoding a polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 5 with at least one amino acid deletion;~~

~~(d)~~(b) ~~a nucleotide sequence~~ encoding a polypeptide as set forth in ~~either SEQ ID NO: 2 or~~ SEQ ID NO: 5 ~~that~~ has~~ving~~ a C- and/or N- terminal truncation;

~~(e)~~(c) ~~a nucleotide sequence~~ encoding a polypeptide as set forth in ~~either SEQ ID NO: 2 or~~ SEQ ID NO: 5 with at least one modification ~~selected from the group consisting of~~ that is a conservative amino acid substitution~~s, amino acid insertions, amino acid deletions~~, C-terminal truncation, ~~and~~ or N-terminal truncation; or

~~(f) a nucleotide sequence of any of (a) - (e) comprising a fragment of at least about 16 nucleotides; and~~

~~(g)~~(d) ~~a nucleotide sequence~~ that hybridizes ~~under at least moderately stringent conditions~~ to the complement of the nucleotide sequence of any of (a) - ~~(f)~~(c) under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences;

wherein the encoded polypeptide ~~has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~ upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation.

7. (Amended) The isolated polypeptide according to Claim 2 or 3, wherein the percent identity is determined using a computer program ~~selected from the group consisting of~~ that is GAP, BLASTP, FASTA, BLASTA, BLASTX, BestFit, ~~and~~ or the Smith-Waterman algorithm.

10. (Amended) The composition of Claim 8, wherein the polypeptide comprises ~~the~~ an amino acid sequence as set forth in ~~either SEQ ID NO: 3 or~~ SEQ ID NO: 6.

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13. (Amended) The polypeptide of Claim 12, wherein the water-soluble polymer is ~~selected from the group consisting of~~ polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols, ~~and~~ or polyvinyl alcohol.

16. (Amended) A polypeptide produced by a process comprising culturing a host cell comprising a vector comprising a nucleic acid molecule comprising a nucleotide sequence ~~selected from the group consisting of~~:

(a) ~~the nucleotide sequence~~ as set forth in ~~either SEQ ID NO: 1 or~~ SEQ ID NO: 4;

(b) ~~the nucleotide sequence~~ of the DNA insert in ATCC Deposit No. PTA-976;

(c) ~~a nucleotide sequence~~ encoding ~~the~~ a polypeptide as set forth in ~~either SEQ ID NO: 2 or~~ SEQ ID NO: 5; ~~and~~ or

(d) ~~a nucleotide sequence~~ that hybridizes ~~under at least moderately stringent conditions~~ to the complement of the nucleotide sequence of any of (a) - (c) under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences, wherein the polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation;

under suitable conditions to express the polypeptide, and optionally isolating the polypeptide from the culture.

17. (Amended) A polypeptide produced by a process comprising culturing a host cell comprising a vector comprising a nucleic acid molecule comprising ~~a nucleotide sequence selected from the group consisting of~~:

(a) a nucleotide sequence encoding a polypeptide that is at least about 70 percent identical to the polypeptide ~~as~~ set forth in ~~either SEQ ID NO: 2 or~~ SEQ ID NO: 5, wherein the encoded polypeptide ~~has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~ upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation;

~~(b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide~~

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~~sequence as set forth in either SEQ ID NO: 1 or SEQ ID NO: 4, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-976, or the nucleotide sequence of (a);~~

~~(c)~~(b) a region of the nucleotide sequence of ~~either SEQ ID NO: 1 or~~ SEQ ID NO: 4, the DNA insert in ATCC Deposit No. PTA-976, or the nucleotide sequence of (a) ~~or (b)~~, wherein the ~~encoding~~ a polypeptide ~~fragment of~~ comprises at least about 25 amino acid residues, and wherein the polypeptide ~~fragment has an activity of the encoded polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~ upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation, or is antigenic; or

~~(d) a region of the nucleotide sequence of either SEQ ID NO: 1 or SEQ ID NO: 4, the DNA insert in ATCC Deposit No. PTA-976, or the nucleotide sequence of any of (a) - (c), comprising a fragment of at least about 16 nucleotides; and~~

~~(e)~~(c) a nucleotide sequence that hybridizes ~~under at least moderately stringent conditions~~ to the complement of the nucleotide sequence of ~~any of (a) - (d)~~ (b) under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences, wherein the polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation;

under suitable conditions to express the polypeptide, and optionally isolating the polypeptide from the culture.

18. (Amended) A polypeptide produced by a process comprising culturing a host cell comprising a vector comprising a nucleic acid molecule comprising a nucleotide sequence ~~selected from the group consisting of~~:

(a) ~~a nucleotide sequence~~ encoding a polypeptide as set forth in ~~either SEQ ID NO: 2 or~~ SEQ ID NO: 5 with at least one conservative amino acid substitution~~, wherein the encoded polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~;

~~(b) a nucleotide sequence encoding a polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 5 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5;~~

~~(c) a nucleotide sequence encoding a polypeptide as set forth in either SEQ ID NO: 2 or SEQ ID NO: 5 with at least one amino acid deletion, wherein the encoded polypeptide has an~~

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~~activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5;~~

~~(d)~~(b) ~~a nucleotide sequence~~ encoding a polypeptide as set forth in ~~either SEQ ID NO: 2 or~~ SEQ ID NO: 5 ~~that~~ hasving a C- and/or N- terminal truncation~~, wherein the encoded polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~;

~~(e)~~(c) ~~a nucleotide sequence~~ encoding a polypeptide as set forth in ~~either SEQ ID NO: 2 or~~ SEQ ID NO: 5 with at least one modification ~~selected from the group consisting of~~ that is a conservative amino acid substitution~~s, amino acid insertions, amino acid deletions~~, C-terminal truncation, ~~and~~ or N-terminal truncation~~, wherein the encoded polypeptide has an activity of the polypeptide set forth in either SEQ ID NO: 2 or SEQ ID NO: 5~~; or

~~(f) a nucleotide sequence of any of (a) - (e) comprising a fragment of at least about 16 nucleotides; and~~

~~(g)~~(d) ~~a nucleotide sequence~~ that hybridizes ~~under at least moderately stringent conditions~~ to the complement of the nucleotide sequence of any of (a) - ~~(f)~~(c) under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences;

wherein the polypeptide upon exposure to mammalian cells, causes an increase in cellular protein tyrosine phosphorylation;

under suitable conditions to express the polypeptide, and optionally isolating the polypeptide from the culture.

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